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# *Ab Initio* and Molecular Mechanics (MM2 and MM3) Calculations of Positively Charged Conjugated Nitrogen-Containing Compounds\*

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## ABSTRACT

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*Ab initio* calculations have been carried out on *s-trans-N*-vinylmethyleammonium, pyridinium, and related compounds to obtain rotational barriers, structures, and vibrational frequencies. The restricted Hartree-Fock (RHF) level of theory with 6-31G\*\* basis set was used for these calculations. In addition, the MM2(91) and MM3(94) force fields have been parameterized to calculate these positively charged nitrogen-containing compounds. A bond order term was incorporated in the force field to reproduce accurately the rotational barriers of *s-trans-N*-vinylmethyleammonium and related compounds. Molecular mechanics geometries and vibrational frequencies compare well with those calculated by *ab initio* methods. © 1996 by John Wiley & Sons, Inc.

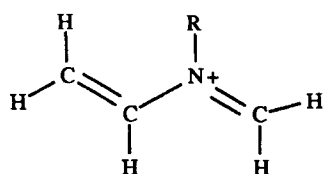
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## Introduction

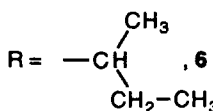
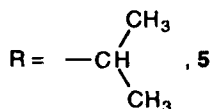
The introduction and widespread use of computational chemistry has had profound effects in the chemical and biomedical sciences. Molecular mechanics methods have been particularly effective in correctly predicting molecular structures that have been used in conformational

\*This article includes Supplementary Material available from the authors upon request or via the Internet at [ftp.wiley.com/public/journals/jcc/suppmat/17/1395](http://ftp.wiley.com/public/journals/jcc/suppmat/17/1395) or <http://www.wiley.com/jcc>

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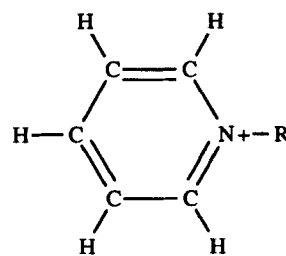
R = H, 1

R = CH<sub>3</sub>, 2R = CH<sub>2</sub>CH<sub>3</sub>, 3R = CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, 4**FIGURE 1.** *s-trans-N*-vinylmethyleammonium and related structures.

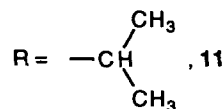
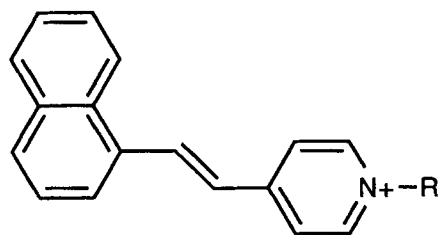
analysis and rational molecular design. Such advances, however, will only continue with the improvement of force fields to include more diverse classes of molecular structures.

We have extended the limits of the MM2(91) and MM3(94) methods<sup>‡</sup> to include cyclic and acyclic positively charged nitrogen-containing compounds by studying *s-trans-N*-vinylmethyleammonium, 1, pyridinium, 7, and some of their derivatives (Figs. 1 and 2). The necessity for developing force fields capable of handling positively charged nitrogen-containing structures stems from our interest in understanding the geometries and preferred conformations of active and inactive naphthylvinylpyridine choline acetyltransferase (ChAT) inhibitors<sup>1-7</sup> (Fig. 3). Inhibition of ChAT interferes with the regular sequence of nerve impulses, and other studies have linked this enzyme with Alzheimer's dementia.<sup>5</sup> Because little structural information about ChAT is available, three-

<sup>‡</sup> The programs MM2(91), which is an extended but otherwise unchanged version of MM2 [N. L. Allinger and Y. Yuh, *QCPE Newsletter*, 12, 395 (1980)], and MM3(94) are available from the Quantum Chemistry Program Exchange, Department of Chemistry, University of Indiana, Bloomington, IN 47401 and from Tripos Associates, Inc., 1699 South Hanley Road, Suite 303, St. Louis, Missouri 63144.



R = H, 7

R = CH<sub>3</sub>, 8R = CH<sub>2</sub>CH<sub>3</sub>, 9R = CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, 10**FIGURE 2.** Pyridinium and related structures.**FIGURE 3.** Naphthylvinylpyridine (NVP) choline acetyltransferase (ChAT) inhibitor.

dimensional quantitative structure activity relationship studies, such as comparative molecular field analysis, involving these inhibitors may be able to elucidate pertinent information on the active site. The success of these studies, of course, is extremely dependent on the robustness and accuracy of molecular mechanics.

The purpose of this study was to obtain the geometries, vibrational frequencies, and conformational energy differences of the title structures and to utilize these results in the formulation of MM2(91) and MM3(94) force fields for positively charged conjugated nitrogen-containing compounds. Little experimental data on these compounds are available; thus, RHF/6-31G\*\*//RHF/6-31G\*\* *ab initio* calculations were carried out on *N*-vinylmethyleammonium, 1, pyridinium, 7, and related structures to acquire the neces-

sary structural information. These quantum mechanical results were then used to augment the missing experimental data in the parameterization process.

## Methodology

The *ab initio* results reported here were obtained with the GAUSSIAN 92<sup>8</sup> suite of programs on an IBM RS/6000 workstation. Optimizations were undertaken at the restricted Hartree-Fock (RHF) level of theory with the standard 6-31G\*\* basis set. For the molecular mechanics calculations, modified versions of MM2(91) and MM3(94) were utilized. The MM2(91) and MM3(94) programs were modified to include new atom types (73 and 111, respectively), which correspond to  $sp^2$  hybridized conjugated charged nitrogens. All molecular mechanical calculations described herein used these modified programs on a Silicon Graphics 4D/310GTX.

The general strategy employed for MM2(91) and MM3(94) parameterization was essentially identical to that previously described for positively charged nonconjugated nitrogen-containing systems.<sup>9</sup> The *ab initio* study initially focused on the barriers to rotation for *N*-methylpyridinium, **8**, *N*-ethylpyridinium, **9**, *N*-*n*-propylpyridinium, **10**, and *N*-isopropylpyridinium, **11**. A reaction coordinate method was used in which the  $C_{sp^2}-N^+-C_{sp^3}-H(C_{sp^3})$  torsion was rotated in 15-degree increments from 0 to 180 degrees. For *N*-methyl-*N*-vinylmethyleammonium, **2**, *N*-ethyl-*N*-vinylmethyleammonium, **3**, *N*-*n*-propyl-*N*-vinylmethyleammonium, **4**, *N*-isopropyl-*N*-vinylmethyleammonium, **5**, and *N*-secbutyl-*N*-vinylmethyleammonium, **6**, the frozen *s-trans* conformation of the parent chain were calculated. In the acyclic cases, the  $C_{sp^2}-N^+-C_{sp^3}-H(C_{sp^3})$  torsion was rotated from 0 to 180 degrees in increments of 15 degrees, where  $C_{sp^2}$  is the interior  $sp^2$  carbon with one attached hydrogen. These calculated barriers were used later in the determination of MM2(91) and MM3(94) torsional parameters. Minima for the *s-trans* structures were located by selecting conformations near valleys in the potential energy surface, releasing any geometrical constraints on these structures and allowing the geometries to fully optimize. After full geometry optimization, vibrational frequency calculations were undertaken to verify that these

structures were indeed minima and to use in parameterization of the MM3(94) frequencies.

## Results and Discussion

### AB INITIO ENERGETICS

The result of the reaction coordinate calculations for *N*-ethylpyridinium, **9**, at the RHF/6-31G\*\* level is shown in Figure 4.<sup>§</sup> The barriers are characteristic of profiles resulting from rotations about dihedral angles involving groups singly bonded to an aromatic ring system. *N*-methylpyridinium, **8**, has a very low barrier to rotation ( $< 0.010$  kcal/mol) about the  $N^+_{sp^2}-C_{sp^2}$  bond implying essentially free methyl group rotation; this is also observed in the all-carbon aromatic analog methylbenzene. The barriers for *N*-ethylpyridinium, **9**, and *N*-*n*-propylpyridinium, **10**, have twofold symmetry, as one would expect, with the minima of these structures occurring at the 90-degree conformers. Maxima are observed at the 0- and 180-degree rotomers and may be attributed to steric interactions between the methylene group of the sidechains and the hydrogens of the aromatic carbon atoms in the pyridinium ring. A shift in the maxima and minima by approximately 30 degrees was noticed for the less sym-

<sup>§</sup> Rotational barriers, structural information, and vibrational frequencies for compounds not reported herein can be obtained as supplemental material.

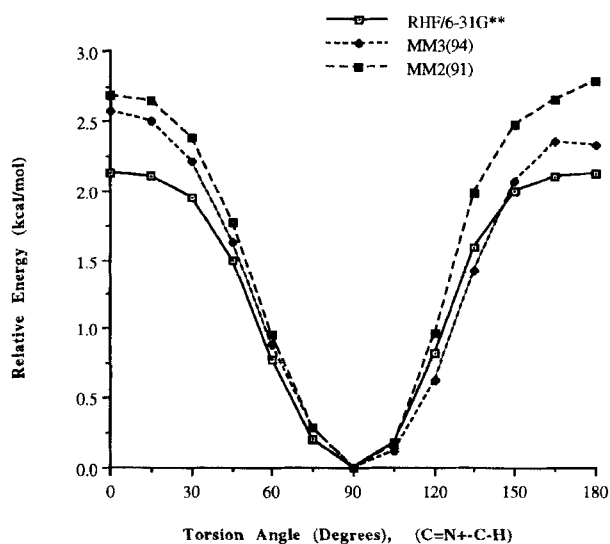


FIGURE 4. RHF / 6-31G\*\* and MM2(91) and MM3(94) sidechain rotational profiles for *N*-ethylpyridinium.

metrical *N*-isopropylpyridinium, **11**. Again, this torsional profile arises from the steric interactions of the methylene groups of the isopropyl sidechain and the hydrogens of the aromatic ring. In this case, however, the steric interactions occur between the methylene group, which is not involved with the reaction coordinate, and the aromatic ring hydrogens.

The acyclic conjugated iminium structures illustrate rotational barriers similar to those seen in compounds such as isoprene and its derivatives.<sup>10</sup> With the *N*-methyl-*N*-vinylmethyleammonium structure, **2**, a preference for the 60- and 180-degree conformer (eclipsing of the  $C_{sp^3}$ -H bond with the  $C_{sp^2}=C_{sp^2}$  bond of the parent chain), characteristic of a symmetric three-fold potential is seen (Fig. 5). However, in the rotational profiles of *N*-ethyl-*N*-vinylmethyleammonium, **3**, and *N*-*n*-propyl-*N*-vinylmethyleammonium, **4**, an energy lowering, however, is observed at the 120-degree conformer (approximately 1.0 kcal/mol lower than the 0-degree conformer). This energy lowering implies an inequality in the  $C_{sp^2}$  atoms of the conjugated chain which, due to symmetry, is observed in the *N*-methyl-*N*-vinylmethyleammonium profile. One can conclude from these rotational profiles that the magnitude of the interaction of the sidechain and the eclipsing  $C_{sp^2}$  atom is dependent on the amount of electron density within the adjacent bond (the bond order). Further exami-

nation of the profiles reveals that interaction with bonds possessing greater double bond character is favored over interaction with bonds having greater single bond character. As for the isopropyl structure, **5**, a shift in the barrier similar to the one observed in *N*-isopropylpyridinium, **10**, is found.

#### AB INITIO STRUCTURES

Once the torsional profiles for the pyridinium derivatives were completed, structures near the global minima were allowed to relax fully to their equilibrium geometries, as described previously. The bond lengths of the resulting minima were then scaled from  $r_e$  to  $r_g$  to be used in MM2(91) and MM3(94) parameterization. Bond length scaling was based on differences in the MM3(94) and RHF/6-31G\*\* bond lengths of compounds similar to those under study (pyridine, ethane, and *n*-vinyl-2-ethylidenimine). The structure of pyridine was used in the scaling of the pyridinium bond lengths, and ethane was selected for scaling of the aliphatic sidechains. MM3(94) was selected as the force field for scaling rather than MM2(91) since MM3(94) is known to reproduce the geometry of pyridine and ethane with greater accuracy. The MM3(94) and RHF/6-31G\*\*//RHF/6-31G\*\* calculated structures of pyridine and ethane are shown in Table I along with the differences, which

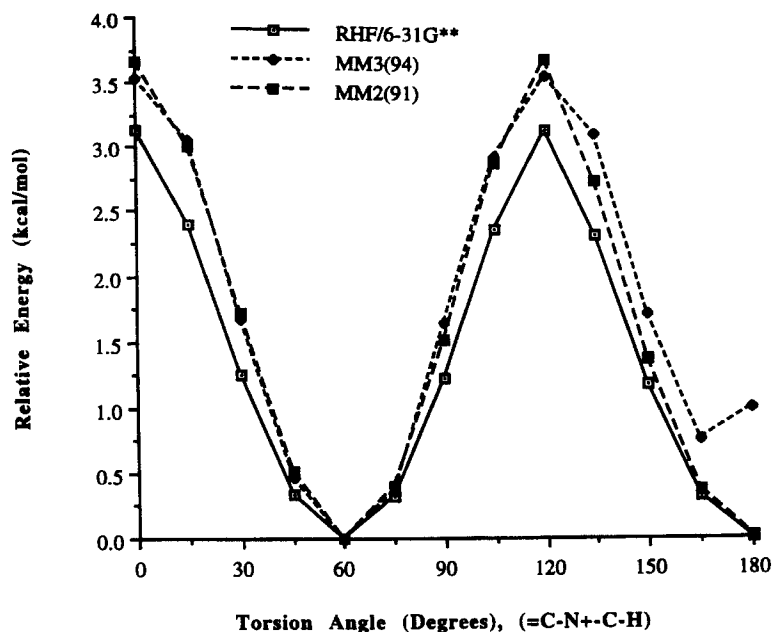
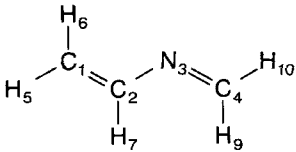
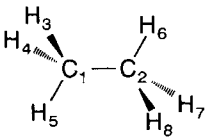
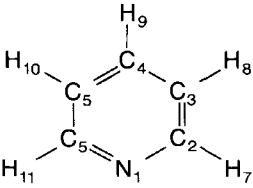


FIGURE 5. RHF/6-31G\*\*, MM2(91), and MM3(94) sidechain rotational profiles for *N*-methyl-*N*-vinylmethyleammonium.

TABLE I.

Scaling factors for *N*-vinylmethyleammonium and pyridinium structures calculated from MM3(94) and RHF / 6-31G\*\* results of pyridine, *N*-vinyl-2-ethylidenimine (*s-trans*), and ethane.

			
Bond Lengths	MM3(94) <sup>a</sup>	RHF / 6-31G** <sup>b</sup>	Difference
C(4) — N(3)	1.3442	1.3205	0.0237
N(3) — C(2)	1.4387	1.4173	0.0214
C(1) — C(2)	1.2869	1.2510	0.0359
C(2) — H(7)	1.1044	1.0752	0.0292
C(1) — H(6)	1.1022	1.0743	0.0279
C(4) — C(8)	1.0994	1.0837	0.0159
			
Bond Lengths	MM3(94) <sup>a</sup>	RHF / 6-31G** <sup>b</sup>	Difference
C(1) — C(2)	1.5313	1.5273	0.0040
C(1) — H(3)	1.1131	1.0857	0.0274
			
Bonds and Angles	MM3(94) <sup>a</sup>	RHF / 6-31G** <sup>b</sup>	Difference
N(1) — C(2)	1.3474	1.3209	0.0265
C(2) — C(3)	1.3960	1.3849	0.0111
C(2) — H(7)	1.1033	1.0767	0.0266
C(3) — C(4)	1.3901	1.3835	0.0066
C(3) — H(8)	1.1029	1.0746	0.0283
C(4) — H(9)	1.1025	1.0759	0.0266
C(2) — N(1) — C(6)	117.25	117.729	— <sup>c</sup>
N(1) — C(2) — C(3)	123.04	123.587	—
N(1) — C(2) — H(7)	117.49	116.195	—
C(2) — C(3) — C(4)	119.38	118.231	—
C(2) — C(3) — H(8)	120.35	120.338	—
C(3) — C(4) — C(5)	117.90	118.634	—
C(3) — C(4) — H(9)	121.05	120.682	—

<sup>a</sup> MM3(94) bond lengths are expressed in angstroms (Å) and are given as  $r_g$  values. The bond angles are reported in degrees (°).

<sup>b</sup> RHF / 6-31G\*\* bond lengths are expressed in angstroms (Å) and are given as  $r_e$  values. The bond values are reported in degrees (°).

<sup>c</sup> Since there was little difference between the MM3(94) and RHF / 6-31G\*\* results for bond angles, no correction factors were determined.

were later used to scale the pyridinium derivatives. Since only minor differences between the RHF/6-31G\*\* and MM3(94) bond angles were observed for pyridine and ethane, the pyridinium bond angles calculated using *ab initio* methods were not scaled.

The scaled results of the RHF/6-31G\*\* calculations for *N*-methylpyridinium, **2**, are shown in Table II. As can be seen, the results are similar to those obtained in other heterocyclic aromatic compounds such as pyridine: the bonds adjacent to the positive nitrogen are equivalent, and the remaining aromatic carbon-carbon bonds are correspondingly equal.

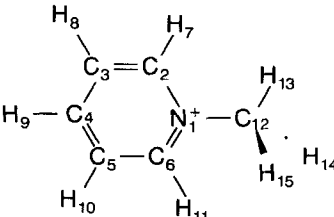
Structural calculations of the acyclic systems were carried out analogously to those of the cyclic structures. *N*-vinyl-2-ethylidenimine (*s-trans*) was used as the structure for scaling the RHF/6-31G\*\*

vinylmethyleammonium results. Calculations similar to those mentioned earlier were undertaken on *N*-vinyl-2-ethylidenimine (*s-trans*) to obtain the results in Table I. Bond length scaling factors were derived from these results and used to scale the *N*-vinylmethyleammonium derivatives. The scaled results for *N*-methyl-*N*-vinylmethyleammonium, **2**, are shown in Table III.

### MM2(91) AND MM3(94) PARAMETERIZATION

Once the *ab initio* results were completed and scaled to the proper bond lengths ( $r_g$ ), reproduction of the energetics and structures was undertaken in the modified MM2(91) and MM3(94) force fields. Additionally, the RHF vibrational frequencies were scaled by 0.9 and modeled in the

**TABLE II.**  
RHF/6-31G\*\*, MM2(91), and MM3(94) structural results for *N*-methylpyridinium.

					
Bond	RHF/6-31G** <sup>a</sup>	MM2(91) <sup>b</sup>	Difference	MM3(94) <sup>b</sup>	Difference
N <sup>+</sup> (1) — C(2)	1.3649	1.3650	0.0001	1.3651	0.0002
N <sup>+</sup> (1) — C(6)	1.3649	1.3647	−0.0002	1.3643	0.0006
N <sup>+</sup> (1) — C(12)	1.4924	1.4964	0.0040	1.4888	−0.0036
		rms diff. <sup>c</sup>	0.0068		0.0054
Bond Angle	RHF/6-31G** <sup>d</sup>	MM2(91) <sup>e</sup>	Difference	MM3(94) <sup>e</sup>	Difference
C(2) — N <sup>+</sup> (1) — C(6)	120.697	120.472	−0.225	120.090	−0.607
C(2) — N <sup>+</sup> (1) — C(12)	120.590	120.841	0.251	120.652	0.062
C(6) — N <sup>+</sup> (1) — C(12)	118.700	118.684	−0.016	119.258	0.558
N <sup>+</sup> (1) — C(2) — C(3)	121.112	120.656	−0.456	120.623	−0.489
N <sup>+</sup> (1) — C(2) — H(7)	116.576	117.585	1.009	115.878	−0.698
N <sup>+</sup> (1) — C(6) — C(5)	121.130	120.751	−0.379	120.743	−0.387
N <sup>+</sup> (1) — C(6) — H(11)	116.574	117.033	0.459	115.374	−1.200
N <sup>+</sup> (1) — C(12) — H(13)	108.945	107.505	−1.440	107.349	−1.596
N <sup>+</sup> (1) — C(12) — H(14)	109.254	109.399	0.145	108.990	−0.264
N <sup>+</sup> (1) — C(12) — H(15)	108.945	107.548	−1.397	107.347	−1.598
		rms diff.	0.619		0.738

<sup>a</sup> RHF/6-31G\*\* bond lengths are given in angstroms (Å) and are scaled to  $r_g$  bond lengths based on MM3(94) calculations of the pyridine and ethane structures.

<sup>b</sup> MM2(91) and MM3(94) bond lengths are given in angstroms (Å) and are reported as  $r_g$  bond lengths.

<sup>c</sup> The rms difference in the calculated bond lengths reported in this table represent the rms difference of all the bonds and not just the rms of those reported.

<sup>d</sup> RHF/6-31G\*\* bond angles are given in degrees (°) and are not scaled to the MM3(94) structures of pyridine and ethane.

<sup>e</sup> MM2(91) and MM3(94) bond angles are given in degrees (°).

MM3(94) force field. Because the positively charged nitrogens are considered to be conjugated,  $\pi$  calculations were invoked in the parameterization scheme. The final MM2(91) and MM3(94) parameter sets for this class of compounds are illustrated in Tables IV and V, respectively.

### MM2(91) AND MM3(94) BOND MOMENTS

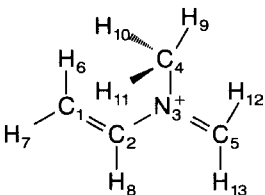
Bond moments were determined and optimized for pyridinium, 7, and *N*-methylpyridinium, 8. Dipole moments obtained from *ab initio* data were used, and the appropriate bond moments in the parameter set were adjusted to reproduce those results. For pyridinium, 7, the *ab initio* dipole value was 1.9320 Debyes and the MM2(91) and MM3(94) values were 1.9540 and 1.9370 Debyes, respectively. For *N*-methylpyridinium, 8, the *ab initio* value was 0.9788 Debyes and the MM2(91)

and MM3(94) values were 0.9780 and 0.9790 Debyes, respectively.

### MM2(91) AND MM3(94) ENERGETICS

With the MM2(91) and MM3(94) parameters provided in Tables IV and V, the *ab initio* barriers to rotation were characterized accurately for both the cyclic and acyclic structures. Unlike the MM2(91) parameterization of these barriers, however, the primary goal in the MM3(94) parameterization was to model the rotational barriers while simultaneously reproducing torsional frequencies. Initial efforts on parameterization of these profiles focused on the barriers of the pyridinium derivatives. The general shape of the curves is reproduced well (as an example, see Figure 4), and the difference between the *ab initio* and molecular mechanics barriers is small; in most cases, it is less

**TABLE III.**  
RHF/6-31G\*\*, MM2(91), and MM3(94) structural results for *s-trans-N*-vinylmethyleammonium.

					
Bond	RHF/6-31G** <sup>a</sup>	MM2(91) <sup>b</sup>	Difference	MM3(94) <sup>b</sup>	Difference
C(2) — N <sup>+</sup> (3)	1.4601	1.4647	0.0046	1.4588	−0.0013
N <sup>+</sup> (3) — C(4)	1.4828	1.5003	0.0175	1.4901	0.0076
N <sup>+</sup> (3) — C(5)	1.3008	1.3008	0.0000	1.3010	0.0002
		rms diff. <sup>c</sup>	0.0068		0.0036
Bond Angle	RHF/6-31G** <sup>d</sup>	MM2(91) <sup>e</sup>	Difference	MM3(94) <sup>e</sup>	Difference
C(1) — C(2) — N <sup>+</sup> (3)	123.971	123.844	−0.127	124.088	0.117
N <sup>+</sup> (3) — C(2) — H(8)	113.161	116.027	2.866	114.247	1.086
C(2) — N <sup>+</sup> (3) — C(4)	119.002	119.010	0.008	119.800	0.798
C(2) — N <sup>+</sup> (3) — C(5)	120.081	121.612	1.531	120.375	0.294
C(4) — N <sup>+</sup> (3) — C(5)	120.918	119.377	−1.541	119.825	−1.093
N <sup>+</sup> (3) — C(4) — H(9)	109.005	109.904	0.899	109.191	0.186
N <sup>+</sup> (3) — C(4) — H(10)	108.594	107.618	−0.976	107.454	−1.140
N <sup>+</sup> (3) — C(4) — H(11)	108.594	107.620	−0.974	107.454	−1.140
N <sup>+</sup> (3) — C(5) — H(12)	120.104	118.747	−1.357	118.633	−1.469
N <sup>+</sup> (3) — C(5) — H(13)	120.230	119.516	−0.714	118.500	−1.730
		rms diff.	1.225		0.953

<sup>a</sup> RHF/6-31G\*\* bond lengths are given in angstroms (Å) and are scaled to  $r_g$  bond lengths based on MM3(94) calculations of the *N*-vinyl-2-ethylidenimine and ethane structures.

<sup>b</sup> MM2(91) and MM3(94) bond lengths are given in angstroms (Å) and are reported as  $r_g$  bond lengths.

<sup>c</sup> The rms difference in the calculated bond lengths reported in this table represent the rms difference of all the bonds and not just the rms of those reported.

<sup>d</sup> RHF/6-31G\*\* bond angles are given in degrees (°) and are not scaled to the MM3(94) structures of pyridine and ethane.

<sup>e</sup> MM2(91) and MM3(94) bond angles are given in degrees (°).

**TABLE IV.**  
**MM2(91) parameter set for cyclic and acyclic conjugated positively charged nitrogen-containing compounds.**

Torsions				$V_1^a$	$V_2$	$V_3$
73	2	2	1	0.00	7.50	1.00
2	2	2	73	0.00	10.00	0.50
2	2	73	2	-0.30	15.00	0.50
2	73	1	1	0.00	-0.10	0.00
2	73	1	5	0.00	0.00	0.00
2	2	73	1	0.00	0.00	0.00
5	2	73	1	0.00	12.20	0.00
2	2	73	23	0.82	6.00	0.00
5	2	73	23	0.00	15.00	0.00
73	2	2	5	0.00	15.00	0.00
2	73	2	5	0.00	14.15	0.70
73	1	1	1	0.00	0.00	-0.10
73	1	1	5	0.00	0.00	0.50
5	1	73	1	0.00	0.00	0.80

Bonds		$K_s^b$	$I_0^c$	SSLOPE	TSLOPE	Bond Moment <sup>d</sup>
23	73	6.52	1.0130	—	—	1.780
2	73	6.10	1.2700	3.5000	0.2100	0.230
1	73	4.20	1.4850	—	—	1.250

Bond Angles		$K_\theta^e$	$\theta_0^f$	
	73	23	0.150	0.00
	2	73	0.050	0.00
2	73	23	0.650	109.80
2	73	2	1.100	120.00
2	2	73	1.200	120.50
73	2	5	0.600	114.40
1	73	2	0.600	113.50
5	1	73	0.750	105.80
73	1	1	0.660	109.50

<sup>a</sup> The units of the Fourier torsional terms ( $V_1$ ,  $V_2$ , and  $V_3$ ) are given in kcal/mol.<sup>b</sup> The units of  $K_s$  are given in mdynes/Å.<sup>c</sup> The units of  $I_0$  are in Å.<sup>d</sup> The bond moment units are in debyes.<sup>e</sup>  $K_\theta$  is expressed in units of mdynes/Å/rad<sup>2</sup>.<sup>f</sup>  $\theta_0$  is given in units of degrees.

than 1 kcal/mol. Since *ab initio* barriers may differ by approximately  $\pm 1.0$  kcal/mol with respect to experiment, this error is acceptable.

Next attempts to model the *ab initio* barriers for the *s-trans* structures were undertaken. The first effort to duplicate these barriers used the parameters optimized for the aromatic structures, which resulted in enormous errors in the *N*-vinylmethylenammonium barriers. It was observed that rotation of the aliphatic sidechains in both the aromatic and conjugated systems was strongly dependent on the bond orders of the adjacent bonds within the parent chain or ring. As a result,

a  $\pi$ -bond order correction to the torsional term, similar to that proposed by Liljefors and Allinger,<sup>10</sup> was added to MM2(91)<sup>11</sup> and MM3(94)<sup>12</sup> specifically for these structures. This correction term modifies the proper  $V_3$  term of the torsion based on the  $\pi$ -bond order of the adjacent bonds. The form of this equation is as follows:

$$V_3(\text{H}-\text{C}_{sp^3}-\text{N}^+_{sp^2}-\text{C}_{sp^2}) \\ = V_3^0(\text{H}-\text{C}_{sp^3}-\text{N}^+_{sp^2}-\text{C}_{sp^2})\rho_{ij} + A(1 - \rho_{ij}) \quad (1)$$

<sup>12</sup> This subroutine is available in the MM3(95) release.



where  $V_3^0$  is the torsional constant for a  $\pi$ -bond of unity,  $\rho_{ij}$  is the  $\pi$ -bond order for the corresponding  $N^+_{sp^2}-C_{sp^2}$  bond, and  $A$  is a constant, which when multiplied by  $(1 - \rho_{ij})$ , is used to scale  $V_3^0$ . Based on the results of the quantum mechanical barrier calculations, values of 0.80 and 0.60 for  $A$  were determined to provide the best model for the barriers to rotation for MM2(91) and MM3(94), respectively. This correction term has only been included for those torsions that contain hydrogens (methylene groups). This was done since the only significant differences discovered were for those compounds whose torsions contained hydrogens. Therefore, the effect is most pronounced in the methyl-substituted structures, **2** and **8**, while the isopropyl-substituted compounds, **5** and **11**, were not significantly influenced by this phenomenon.

### MM2(91) AND MM3(94) STRUCTURE

Structural modeling of the scaled *ab initio* results concentrated primarily on the aromatic ring structures with less emphasis on the *s-trans* non-ring structures. The results of the MM2(91) and MM3(94) parameterizations of *N*-methylpyridinium, **8**, and *N*-methyl-*N*-vinylmethylenammonium, **2**, are shown in Tables II and III. In these results, the principal differences arise in the reproduction of the  $N^+_{sp^2}-C_{sp^2}$  bond lengths for both the cyclic and acyclic structures. The range of the  $N^+_{sp^2}-C_{sp^2}$  bond lengths was large: from approximately 1.354 Å in the cyclic system to 1.300 Å and 1.4500 Å in the acyclic structures. Differences of this magnitude could not be reproduced accurately in all cases. Initially, MM2(91) and MM3(94) stretching parameters were optimized to reproduce the bond lengths of the cyclic compounds. Final parameter optimization included both cyclic and acyclic compounds. The resulting parameters give good root mean square (rms) deviations for the aromatic bond lengths, while the conjugated systems have only satisfactory rms deviations.

Bond angle calculations in MM2(91) and MM3(94) resulted in the same conflict: Both cyclic and acyclic systems could not be reproduced simultaneously. Again greater attention was given to modeling the cyclic structures. Consequently, the cyclic compounds, as seen in Table II, illustrate lower deviations of the two classes (usually less than 1.0 degree). The acyclic systems, nonetheless, show much higher deviation, usually greater than 1 degree (Table III). The most difficult bond angle

to reproduce was the  $N^+_{sp^2}-C_{sp^3}-H$  bond angle. In the case of the aromatic compounds, this angle was trivial to reproduce since all  $N^+_{sp^2}-C_{sp^3}-H$  bond angles were equivalent and constrained by the ring system. The acyclic systems, however, contained nonequivalent  $N^+_{sp^2}-C_{sp^3}-H$  bond angles as a result of differences in bond orders of the  $N^+_{sp^2}-C_{sp^3}$  bonds. In this case, a model was formulated in which differences due to this nonequivalence were averaged over each of the  $N^+_{sp^2}-C_{sp^3}-H$  angles. To account for this nonequivalency, incorporation of a bond order correction to the bending terms, similar to the torsional correction term, may be necessary.

### MM3(94) VIBRATIONAL FREQUENCIES

*Ab initio* vibrational frequencies were reproduced well with MM3(94). All of the rms differences were less than 60  $\text{cm}^{-1}$ . In this report, only pyridinium, **7**, *N*-methylpyridinium, **8**, *s-trans-N*-vinylmethylenammonium, **1**, and *s-trans-N*-methyl-*N*-vinylmethylenammonium, **2**, are discussed. A few of the out-of-plane and in-plane bending modes in both pyridinium, **7**, and *N*-methylpyridinium, **8**, are either too high or too low. Because these modes are associated with parameters that do not have frequencies that involve the charged nitrogen atom type, one cannot alter these parameters. Pyridinium, **7**, with a rms deviation of 41.1  $\text{cm}^{-1}$ , compares reasonably well with the analog benzene whose rms deviation is 60  $\text{cm}^{-1}$ .

For *N*-vinylmethylenammonium, **1**, the  $N^+-H$  bending mode is calculated too low by MM3(94). Because this mode is found only in the spectrum of *N*-vinylmethylenammonium, the parameters associated with this particular mode could have been optimized further (however, only at the expense of altering other modes). All other vibrations involving MM3(94) with charged nitrogen in *N*-vinylmethylenammonium have frequencies that show good agreement with the corresponding *ab initio* calculated frequency. In both the spectrum of *N*-vinylmethylenammonium, **1**, and *N*-methyl-*N*-vinylmethylenammonium, **2**, a few modes exist which illustrate frequency differences of  $\pm 100 \text{ cm}^{-1}$  between the *ab initio* and the corresponding MM3(94) calculated value. These modes are associated with previously optimized parameters and, therefore, no modifications of these parameters could be made.

**TABLE V.**  
**MM3(96) parameter set for cyclic and acyclic positively charged nitrogen-containing compounds.**

Torsions				$V_1^a$	$V_2$	$V_3$
111	2	2	1	0.00	7.50	1.00
2	2	2	111	1.00	15.00	1.50
2	2	111	2	-0.75	15.00	-0.50
2	111	1	1	0.00	0.00	0.00
2	111	1	5	0.00	0.50	0.00
2	2	111	1	0.00	1.00	0.00
5	2	111	1	0.00	12.20	0.00
2	2	111	23	0.82	6.00	0.00
5	2	111	23	0.00	9.00	0.00
111	2	2	5	0.00	12.61	-1.06
2	111	2	5	0.00	15.00	0.00
111	1	1	1	-0.40	0.00	-1.40
111	1	1	5	0.00	0.00	0.40
5	1	111	1	0.00	0.00	0.60

Bonds		$K_s^b$	$I_0^c$	SSLOPE	TSLOPE	Bond Moment <sup>d</sup>
23	111	6.52	1.0130	—	—	0.200
2	111	8.30	1.2739	3.5000	0.2166	1.000
1	111	5.50	1.4750	—	—	1.290

Electropositive Term				Bond Length <sup>e</sup>	
1	1	111	1	0.01540	

Bond Angles			$K_\theta^f$	$\theta_0^g$
	111	23	0.150	
	111	2	0.050	
	2	111	0.050	
2	111	23	0.750	109.80
2	111	2	0.900	120.00
2	2	111	0.750	118.00
111	2	5	0.550	110.50
1	111	2	0.800	119.00
5	1	111	0.950	104.50
111	1	1	0.980	108.64

Bond	AETH <sup>h</sup>	ABENZ <sup>i</sup>	PCB <sup>j</sup>	PDB <sup>k</sup>	EISO <sup>l</sup>	ECONJ <sup>m</sup>	RISO <sup>n</sup>	RCONJ <sup>o</sup>	
2	111	2.307	2.161	0.238	0.740	131.88	113.49	1.262	1.445

<sup>a</sup> The units of the Fourier torsional terms ( $V_1$ ,  $V_2$ , and  $V_3$ ) are given in kcal/mol.<sup>b</sup> The units of  $K_s$  are given in mdynes/Å.<sup>c</sup> The units of  $I_0$  are in Å.<sup>d</sup> The bond moment units are in Debyes.<sup>e</sup> The electropositive term is in Å.<sup>f</sup>  $K_\theta$  is expressed in units of mdynes/Å/rad<sup>2</sup>.<sup>g</sup>  $\theta_0$  is given in units of degrees.<sup>h</sup> Constant a in ethylene-type bond.<sup>i</sup> Constant a in benzene-type bond.<sup>j</sup> Proportionality constant (resonance integral to overlap integral).<sup>k</sup> Modified reciprocal quantum Bohr radius.<sup>l</sup> Localized C=N<sup>+</sup> bond energy (kcal/mol).<sup>m</sup> Delocalized C=N<sup>+</sup> bond energy (kcal/mol).<sup>n</sup> Localized C=N<sup>+</sup> bond length (Å).<sup>o</sup> Delocalized C=N<sup>+</sup> bond length (Å).

## Conclusions

*Ab initio* calculations at the RHF level of theory utilizing the 6-31G\*\* basis set have been undertaken on cyclic and acyclic positively charged conjugated nitrogen-containing compounds to supplement missing experimental data. The results of these calculations have been used in the formulation of MM2(91) and MM3(94) force fields for the title compounds. Barriers to rotation and structural features were calculated. The results of the *ab initio* reaction coordinate calculations verified trends that were postulated from other cyclic and acyclic structures: The molecular systems with higher symmetry produce highly symmetric sidechain rotational barriers. Barrier heights and general curve shape may be attributed to the bond order of the  $N^{+}_{sp^2}-C_{sp^2}$  bonds within these systems. The trends in the minimized geometry corresponded well with those found in the cyclic and acyclic uncharged nitrogen species and thus seemed reasonable.

With the addition of an  $N^{+}_{sp^2}$  atom type, MM2(91) and MM3(94) force fields were formulated with the aid of the *ab initio* calculations. The weight of their parameterization rested principally on the cyclic systems. Barriers to rotation for the cyclic compounds were reproduced well. Only after the addition of a bond order correction term for the corresponding  $V_3$  torsional term could the sidechain rotational barriers for the acyclic systems be reproduced reasonably. The geometries from

MM2(91) and MM3(94) are in reasonable agreement with the *ab initio* results, again with the emphasis placed on accurately calculating the cyclic rather than the acyclic systems. For MM3(94), the vibrational frequencies are well reproduced, especially for the cyclic cases.

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